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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/052,417	01/17/2002	David Harrow Gelfand	022101-000320US	4095

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TOWNSEND AND TOWNSEND AND CREW, LLP
2 EMBARCADERO CENTER, 8TH FLOOR
SAN FRANCISCO, CA 94111

EXAMINER	
SITTON, JEHANNE SOUAYA	
ART UNIT	**PAPER NUMBER**
1634	
MAIL DATE	**DELIVERY MODE**
04/10/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/052,417	GELFAND ET AL.	
	Examiner	Art Unit	
	Jehanne S. Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *21 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6,7,11-13,16,17,21-23,26,31-35,39-41,45,46,50 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11-2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1-3, 6-7, 11-13, 16-17, 21-23, 26, 31-35, 39-41, 45-46, and 50-51 are .

DETAILED ACTION

1. Currently, claims 1-3, 6-7, 11-13, 16-17, 21-23, 26, 31-35, 39-41, 45-46, and 50-51 are pending and under consideration in the instant application. The amendments and arguments have been thoroughly reviewed but are insufficient to place the instant application in condition for allowance. The following rejections are either reiterated or newly applied as necessitated by amendment. This action is Non-FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

3. Claims 1-3, 6-7, 11-13, 16-17, 21-23, 26, 31, 33-35, 39-41, and 45-46 are rejected under 35 USC 103(a) as being unpatentable over Brandis I (Brandis et al; US Patent 6,265,193) in view of Baker (Baker et al; US Patent 5,571,706) as evidenced by Cormier (Cormier et al; US Patent 5,418,155).

Brandis I teaches and claims mutant DNA polymerases having at least one mutation at position 681 with respect to Taq DNA polymerase, wherein the mutant DNA polymerase has at least 2 fold reduced discrimination against the incorporation of a fluorescein type dye labeled nucleotide as compared to a naturally occurring DNA polymerase (see claims 1-13, col. 6, lines 4-39, col. 8, Tables 1 and 2 at cols 17-22).

With regard to claims 1-3, 6-7, 33-35, 39-41, and 45-46, Brandis I teaches making the specific mutants in *Taq* polymerase, which comprises SEQ ID NOS 1-3, as acknowledged by the instant specification at page 15, Brandis I teaches making a number of mutants at position 681 of *Taq*, which have at least 3 fold lower discrimination (table 2, cols 21-22). Brandis I teaches

kits comprising the mutant polymerase and a flouorescently labeled nucleotide dye (claims 6-9), flourescein type dyes (col. 4), and nucleotides which are any naturally occurring nucleotides or analogs such as 2',3' dideoxynucleotides (chain terminator) (col. 4, lines 35-39). Brandis I teaches that sequence homology between DNA polymerases permits corresponding positions to be assigned to amino acid residues for DNA polymerases other than Taq.

With regard to claims 11-13 and 16-17, Brandis I teaches providing polynucleotides encoding the mutant polymerases (abstract, all of col. 11, especially lines 40-45).

With regard to claims 21-23, 26-27, and 31 Brandis I teaches to use the mutant polymerases in methods of Sanger sequencing such as dideoxy nucleotide chain termination, PCR, polynucleotide labeling, and minisequencing.

With regard to the various independent claims and dependent which recite that the amino acid at position 4 (exemplified by position 681 in Taq by BrandisI) is Arg (R), Brandis I does not teach actually making or testing this particular mutant, but does list the amino acids in Table 2, columns 21 and 22. Further, Baker teaches that "It is well known in the biological arts that conservative amino acid substitutions can be made in protein sequences without affecting the function of the protein" (see col 10, lines 4-10). As evidenced by Cormier, standard conservative groups of amino acids include uncharged polar amino acid group which contains G, S, T, C N, Q and the basic amino acid group which contains K, R, and H. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have constructed the particular R mutant in the thermostable polymerase of Brandis I and to have used such mutant as taught by Brandis I in view of the teachings of Brandis I and Baker. Brandis I specifically teaches that the basic amino acid K and H possessed reduced discrimination as did

the polar uncharged amino acids S, C, N, T and that most of the mutants have 3 fold lower discrimination. Although Brandis I does not teach having made the mutants, Brandis I does provide motivation to make them as they are specifically enumerated in the disclosure of Brandis I. Further, Baker teaches that "It is well known in the biological arts that conservative amino acid substitutions can be made in protein sequences without affecting the function of the protein". In view of the teachings of Brandies and Baker, the ordinary artisan would have had a reasonable expectation of success that the particular R mutant would have possessed reduced discrimination given that 16 of 19 possible amino acid mutants made by Brandis I possessed this property and that other amino acids in the same group as R, possessed this property. The ordinary artisan would have been motivated to make the additional amino acid mutants Q and R taught by Brandis I for the purpose of providing a number of mutant polymerases with reduced discrimination against incorporation of a fluorescein type dye labeled nucleotide as taught by Brandis I. Not only would it have been "obvious to try" to make and use the claimed mutants as Brandis I provides specific teaching and motivation to make such mutations in thermostable polymerases, but the prior art of both Brandis I and Baker provide for a reasonable expectation of success. The results would have been predictable to one of ordinary skill in the art (see Examination Guidelines for Determining Obviousness Under 35 USC 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.* Federal Register, Vol 72, No 195, October 2007).

4. Claims 1-3, 6-7, 11-13, 16-17, 21-23, 26, 31, 33-35, 39-41, and 45-46 are rejected under 35 USC 103(a) as being unpatentable over Brandis II (Brandis et al; US PreGrant Publication

2002/0164591) or Brandis III (Brandis et al; US PreGrant Publication 2006/0088879), each in view of Baker as evidenced by Cormier.

Brandis II and III each teaches and claims mutant DNA polymerases having at least one mutation at position 681 with respect to Taq DNA polymerase, wherein the mutant DNA polymerase has at least 2 fold reduced discrimination against the incorporation of a fluorescein type dye labeled nucleotide as compared to a naturally occurring DNA polymerase (see claims 1-8, 15, Tables 1 and 2).

With regard to claims 1-3, 6-7, 33-35, 39-41, and 45-46, Brandis II and III each teaches making the specific mutants in Taq polymerase, which comprises SEQ ID NOS 1-3, as acknowledged by the instant specification at page 15. Brandis II and III each teaches making a number of mutants at position 681 of Taq, which have at least 3 fold lower discrimination (table 2,). Brandis II and III each teaches kits comprising the mutant polymerase and a flouorescently labeled nucleotide dye, flourescein type dyes, and nucleotides which are any naturally occurring nucleotides or analogs such as 2',3' dideoxynucleotides (chain terminator). Brandis II and III teach that sequence homology between DNA polymerases permits corresponding positions to be assigned to amino acid residues for DNA polymerases other than Taq.

With regard to claims 11-13 and 16-17, Brandis II and III each teaches providing polynucleotides encoding the mutant polymerases (abstract, claim 9 of Brandis II)

With regard to claims 21-23, 26-27, and 31 Brandis II teaches to use the mutant polymerases in methods of Sanger sequencing such as dideoxy nucleotide chain termination, PCR, polynucleotide labeling, and minisequencing.

With regard to the various independent claims and dependent which recite that the amino acid at position 4 (exemplified by position 681 in Taq by Brandis II and III) is Arg (R), Brandis II and II do not teach actually making or testing this particular mutant, but do list the amino acids in Table 2. Further, Baker teaches that "It is well known in the biological arts that conservative amino acid substitutions can be made in protein sequences without affecting the function of the protein" (see col 10, lines 4-10). As evidenced by Cormier, standard conservative groups of amino acids include uncharged polar amino acid group which contains G, S, T, C N, Q and the basic amino acid group which contains K, R, and H. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have constructed the particular R and Q mutants in the thermostable polymerase of Brandis II or III and to have used such mutants as taught by Brandis II or III in view of the teachings of Brandis II or III and Baker. Brandis II and III specifically teach that the basic amino acid K and H possessed reduced discrimination as did the polar uncharged amino acids S, C, N, T and that most of the mutants have 3 fold lower discrimination. Although Brandis II or III do not teach having made the mutants, Brandis II and III do provide motivation to make them as they are specifically enumerated in the disclosure. Further, Baker teaches that "It is well known in the biological arts that conservative amino acid substitutions can be made in protein sequences without affecting the function of the protein". In view of the teachings of Brandis II and III and Baker, the ordinary artisan would have had a reasonable expectation of success that the R mutant would have possessed reduced discrimination given that 16 of 19 possible amino acid mutants made by Brandis II or III possessed this property and that other amino acids in the same group as R, possessed this property. The ordinary artisan would have been motivated to make the additional

amino acid mutant R taught by Brandis II or III for the purpose of providing a number of mutant polymerases with reduced discrimination against incorporation of a fluorescein type dye labeled nucleotide as taught by Brandis II or III. Not only would have been "obvious to try" to make and use the claimed mutants as Brandis II or III provides specific teaching and motivation to make such mutations in thermostable polymerases, but the prior art of both Brandis II or III and Baker provide for a reasonable expectation of success. The results would have been predictable to one of ordinary skill in the art (see Examination Guidelines for Determining Obviousness Under 35 USC 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.* Federal Register, Vol 72, No 195, October 2007).

5. Claims 32, and 50-51 are rejected under 35 USC 103(a) as being unpatentable over Brandis I, II, or III each in view Gelfand (US Patent 5,939,292) and Baker as evidenced by Cormier.

Brandis I, II, and III teach mutant DNA polymerases having at least one mutation at position 681 with respect to Taq DNA polymerase, wherein the mutant DNA polymerase has at least 2 fold reduced discrimination against the incorporation of a fluorescein type dye labeled nucleotide as compared to a naturally occurring DNA polymerase. Brandis I, II, and III teach kits comprising the mutant polymerase and a flouorescently labeled nucleotide dye, flourescein type dyes, and nucleotides which are any naturally occurring nucleotides (encompasses dNTP and rNTP).

With regard to claims 32 and 50-51, Brandis I, II and III teach to provide mutant polymerases comprising other mutations in addition to the discrimination mutations such as

those at position 681 of Taq polymerase, including mutants outside the discrimination regions (col. 10, lines 9-23, Table 2, cols 19-22). Brandis I, II and III teach mutations at position 615 of Taq polymerase (instant SEQ ID NOS 18). Brandis I, II or III do not specifically teach a polymerase comprising *both* a mutation at position 681 and a mutation at position 615, however Gelfand teaches to use modified DNA polymerases with enhanced efficiency for incorporating unconventional nucleotides, such as ribonucleotides, using a polymerase with a mutation at position 615, corresponding to Taq polymerase, in methods of DNA sequencing (see abstract, cols 2-3). Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to provide a mutant DNA polymerase with both a mutation at position 681 and 615, relative to Taq, both taught by Brandis, in the mutant polymerases of Brandis I , II or III for use in the sequencing methods or primer extension (minisequencing) methods taught by Brandis I, II or III because Gelfand teaches that the mutation at position 615 in a DNA polymerase provides for DNA polymerases that enable alternative nucleic acid synthesis methods for accurate and cost effective nucleic acid DNA sequence analysis. It would have further been prima facie obvious to the ordinary artisan at the time the invention was made to provide such mutant polymerases and a ribonucleotide labeled with a fluorescein type family dye for the purposes of making the methods of Brandis I, II or III, each in view of Gelfand more convenient to perform.

With regard to the various independent claims and dependent which recite that the amino acid at position 4 (exemplified by position 681 in Taq by Brandis) is Arg (R), Brandis does not teach actually making or testing this particular mutant, but do list the amino acids in Table 2. Further, Baker teaches that "It is well known in the biological arts that conservative amino acid

substitutions can be made in protein sequences without affecting the function of the protein" (see col 10, lines 4-10). As evidenced by Cormier, standard conservative groups of amino acids include uncharged polar amino acid group which contains G, S, T, C N, Q and the basic amino acid group which contains K, R, and H. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have constructed the particular R and Q mutants in the thermostable polymerase of Brandis and Gelfand and to have used such mutants as taught by Brandis in view of the teachings of Brandis and Baker. Brandis specifically teach that the basic amino acid K and H possessed reduced discrimination as did the polar uncharged amino acids S, C, N, T and that most of the mutants have 3 fold lower discrimination. Although Brandis does not teach having made the mutants, Brandis does provide motivation to make them as they are specifically enumerated in the disclosure. Further, Baker teaches that "It is well known in the biological arts that conservative amino acid substitutions can be made in protein sequences without affecting the function of the protein". In view of the teachings of Brandis and Baker, the ordinary artisan would have had a reasonable expectation of success that the particular R and Q mutants would have possessed reduced discrimination given that 16 of 19 possible amino acid mutants made by Brandis possessed this property and that other amino acids in the same group as R possessed this property. The ordinary artisan would have been motivated to make the additional amino acid mutant R taught by Brandis for the purpose of providing a number of mutant polymerases with reduced discrimination against incorporation of a fluorescein type dye labeled nucleotide as taught by Brandis. Not only would have been "obvious to try" to make and use the claimed mutants as Brandis provides specific teaching and motivation to make such mutations in thermostable polymerases, but the prior art of both Brandis

and Baker provide for a reasonable expectation of success. The results would have been predictable to one of ordinary skill in the art (see Examination Guidelines for Determining Obviousness Under 35 USC 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.* Federal Register, Vol 72, No 195, October 2007).

Response to Arguments and Declaration under 37 CFR 1.132

6. The response traverses the rejections over Brandis and asserts that the effect of the R mutation was unexpectedly good and therefore deserving of a patent. At page 13, the response asserts that the rejection clearly relies on the quotation from Baker as evidence for a reasonable expectation of success. This argument has been thoroughly reviewed but was not found persuasive. It is noted that the quotation set forth in the response ignores a key point made in the rejection. The rejection states: "The ordinary artisan would have had a reasonable expectation of success that the R mutant would have possessed reduced discrimination *given that 16 of 19 possible amino acid mutants made by Brandis [I or II or III] possessed this property* and that other amino acids in the same group as R, possessed this property in view of the teachings of Baker." Accordingly, the rejection in fact relied on both the teachings of Brandis and Baker in making the argument regarding a reasonable expectation of success. The rejection made no conclusion that R would have the same level of discrimination as K and H, but that it would be reasonable to expect that R would exhibit reduced discrimination in view of the teachings of Brandis and Baker.

The response further asserts that the Gelfand Declaration provides data showing R produced "surprisingly" good results, especially when one takes into account the quotation from

Baker. The response further cites the Schoenbrunner Declaration, paragraph 8. This argument as well as the Schoenbrunner declaration paragraphs 7 and 8, regarding the expectation of levels of discrimination for conservative amino acid substitutions and the citation of Baker, have been thoroughly reviewed but were not found persuasive. Regarding the issue of the level of reduction in discrimination and the response and declaration relying on the Baker reference, it is relevant to point out the teachings of Brandis. Brandis teaches 1) at col 6, lines 27-37 "The precise degree of discrimination will also vary in accordance with the specific fluorescently labeled nucleotide assayed, e.g. variations in base, dye, or linker. Mutant DNA polymerase of the invention may exhibit anywhere from a slight reduction in discrimination… to a complete elimination of discrimination"; 2) as can be seen from the E681 mutants in table 2 taught by Brandis, although all 16 of the amino acids tested showed a reduction in discrimination, some amino acids within the same family showed improved reduction in discrimination over others (see I vs V and L vs G and A; M vs S, C, N and T; W vs Y). Accordingly, contrary to the assertions made in the response and declaration, it does not appear unexpected that some conservative amino acid substitutions would possess a greater reduction in discrimination than other amino acids within the same group given the teachings of Brandis.

At page 14, the response asserts that one of ordinary skill would not have expected a dramatic change in ranking of substitutions between the Brandis and Gelfand assays. The response cites the Schoenbrunner declaration paragraph 10 which points out that the difference in nucleotides between the Brandis and Gelfand assays is a 3' hydroxyl, whereas discrimination against 3' deoxy nucleotides is mediated by the nature of the amino acid at position 667 of Taq, not position 681. The response further cites paragraph 11of the declaration which states that the

labels used in the two assays was "relatively similar", the difference being two chloro molecules and that "while one would not expect to be able to directly compare quantities between two different assays…one would expect that the ranking of the amino acid substitutions would be similar when the assays use similar labeled nucleotides as is the case here….In view of the similarity between the HEX and TET labels, I would not have expected the relative discrimination between HEX and TET labeled nucleotides to be significantly different between different amino acid substitutions " The response then states at page 15 "while levels may change, it is not clear that relative rankings would change". The response also argues that Brandis teachings include very significant possible variation in nucleotide labels, including non-fluorescein labels and that the data presented in the Gelfand Declaration represents unexpected results. This argument as well as the declaration have been thoroughly reviewed but were not found persuasive. Although the response and declaration point out the difference in structure between the TET and HEX labels, neither the response nor the declaration provide any scientific reasoning as to how or why this difference in structure would not be expected to change the rankings of the amino acid substitutions. In fact, when one compares the H, K, and M substitutions between the Brandis and Gelfand assays, it is clear that in fact, the rankings do change. The difference between the assays are the polymerase, the nucleotide, and the label. As noted by the response, in the assay of Brandis, the M substitution was the best option tested, which performed 47 times better than wildtype enzyme, while H performed 7 times better than wildtype and K performed 6 times better than wildtype, respectively. Conversly, in the Gelfand assay K exhibited more reduced discrimination than M. Additionally, comparing other amino acid substitutions in common between the two assays, G, L, and W also performed better than M

in the Gelfand assay but not in the Brandis assay. Accordingly, applicants arguments that the unexpected results were due to R, and that this was "surprising" is not found persuasive because 1) the teachings of Brandis illustrate that different amino acids within the same group exhibited more reduced discrimination than others and 2) the rankings between the same amino acid substitutions in the Gelfand and Brandis assays did in fact change. It relevant to point out that while applicants argue that "a polymerase with the R substitution" produces unexpectedly superior results" , as specifically noted in the MPEP, the scope of the unexpected results must be commensurate in scope with the claimed invention.

716.02(d) Unexpected Results Commensurate in Scope With Claimed Invention: Whether the unexpected results are the result of unexpectedly improved results or a property not taught by the prior art, the "objective evidence of nonobviousness must be commensurate in scope with the claims which the evidence is offered to support." In other words, the showing of unexpected results must be reviewed to see if the results occur over the entire claimed range. In re Clemens, 622 F.2d 1029, 1036, 206 USPQ 289, 296 (CCPA 1980) (Claims were directed to a process for removing corrosion at "elevated temperatures" using a certain ion exchange resin (with the exception of claim 8 which recited a temperature in excess of 100C). Appellant demonstrated unexpected results via comparative tests with the prior art ion exchange resin at 110C and 130C. The court affirmed the rejection of claims 1-7 and 9-10 because the term "elevated temperatures" encompassed temperatures as low as 60C where the prior art ion exchange resin was known to perform well. The rejection of claim 8, directed to a temperature in excess of 100C, was reversed.). See also In re Peterson, 315 F.3d 1325, 1329-31, 65 USPQ2d 1379, 1382-85 (Fed. Cir. 2003) (data showing improved alloy strength with the addition of 2% rhenium did not evidence unexpected results for the entire claimed range of about 1-3% rhenium); In re Grasselli, 713 F.2d 731, 741, 218 USPQ 769, 777 (Fed. Cir. 1983) (Claims were directed to certain catalysts containing an alkali metal. Evidence presented to rebut an obviousness rejection compared catalysts containing sodium with the prior art. The court held this evidence insufficient to rebut the prima facie case because experiments limited to sodium were not commensurate in scope with the claims.

In the instant case, since the Gelfand and Brandis assays were not the same, and in view of the fact that Brandis teaches that the precise degree of discrimination will vary due to assay conditions, it is not clear that the "surprising superiority" of the Arginine substitution is not

attributable to the particular assay conditions. As such, the claims are not commensurate in scope.

At page 7, the response asserts that it is not clear why one of ordinary skill in the art would make the R substitution if one would have expected no better results than Brands teaches for K or H, and again cites Baker. This argument has been thoroughly reviewed but was not found persuasive. As noted above, Brandis teaches in table 2 that although all 16 of the amino acids tested showed a reduction in discrimination, some amino acids within the same family showed improved reduction in discrimination over others (see I vs V and L vs G and A; M vs S, C, N and T; W vs Y). Further, Brandis teaches that the precise degree of discrimination will vary with assay conditions. In view of these teachings, the ordinary artisan would not have assumed that the R mutant would necessarily behave "no better... than… K or H" and would have been motivated to make additional mutants under varying conditions to arrive at mutant polymerases that would function as taught by Brandis. The response further asserts that Brandis ranks the amino acid mutations made and asks why one of ordinary skill in the art would make the R mutant when M showed the best activity. This argument has been thoroughly reviewed but was not found persuasive. As set forth in the MPEP 2123(II):

> Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). "A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." In re Gurley, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994)

Accordingly, the rejection is maintained.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claim 31 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 13-16, 20-24, 27-32, 36-44 and 48-52 of copending Application No. 09/823,649,(now US Patent 7,179,590) and Giardano (US Patent 6,107,029).

Claim 31 is drawn to a method of producing labeled DNA by providing a mutant thermostable DNA polymerase comprising LSX[RQ]L[AS]IPXXE, a flourescein family dye labeled nucleotide and performing a DNA synthesis reaction. The instant specification defines a "DNA synthesis reaction" to encompass PCR, SDA, transcription mediated amplification, primer extension, and reverse transcription.

The claims of the '649 application are directed to methods of reverse transcription using a mutant thermostable polymerase which comprises L[SA]X[-EAGPD][LI][SA]XXXXE and treating a reaction mixture to initiate synthesis of an extension product to provide a cDNA. The claims further limit the polymerase to a mutant thermostable polymerase such as *Thermus thermophilus*, which has an I at position 7 and a P at position 8 of instantly claimed SEQ ID NO:

1, as well as defining claimed polymerases in terms of additional polymerases such as *Thermus specie Z05* (see table 1). Accordingly, it is clear that the mutant polymerases in the instant claims and the claims of the '649 application are coextensive in scope. The claims differ in that the claims of the '649 application do not provide for a fluorescein family dye labeled nucleotide, however Giordano teaches that synthesizing labeled cDNA from an RNA molecule allows use of the cDNA to screen a library of genes thought to contain the gene encoding an RNA of interest (see col 10, lines 3-8). Additionally, Giordano teaches the use of labels such as fluorescein dyes (col. 7, lines 15-20). Therefore, it would have been prima facie obvious to one of one of ordinary skill in the art at the time the invention was made to modify the DNA synthesis reaction of '649 to label cDNA molecules as taught by Giordano. The ordinary artisan would have been motivated to produce labeled cDNA in the methods of '649 for the purpose of providing cDNA which could be used to screen a library of genes for an RNA of interest as taught by Giordano.

The response does not provide any arguments regarding the instant Obviousness type Double Patenting Rejection.

Conclusion

9. No claims are allowed.

10. It is noted that the filing of a declaration under 37 CFR 1.131 cannot be used to swear behind claims directed to subject matter which is claimed by the '193 patent. See MPEP 715 II:

An affidavit or declaration under 37 CFR 1.131 is not appropriate in the following situations:...
(B) Where the reference U.S. patent or U.S. patent application publication claims the same patentable invention. See MPEP § 715.05 for a discussion of "same patentable invention" and MPEP *> Chapter 2300<.

With regard to claims directed to subject matter claimed in a Publication for Patent, see MPEP 715.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday, Tuesday and Thursday from 9:00 AM to 3:00 PM.

NOTE: The examiner will be on Maternity Leave April to August 2009.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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/Jehanne Sitton/
Primary Examiner
Art Unit 1634